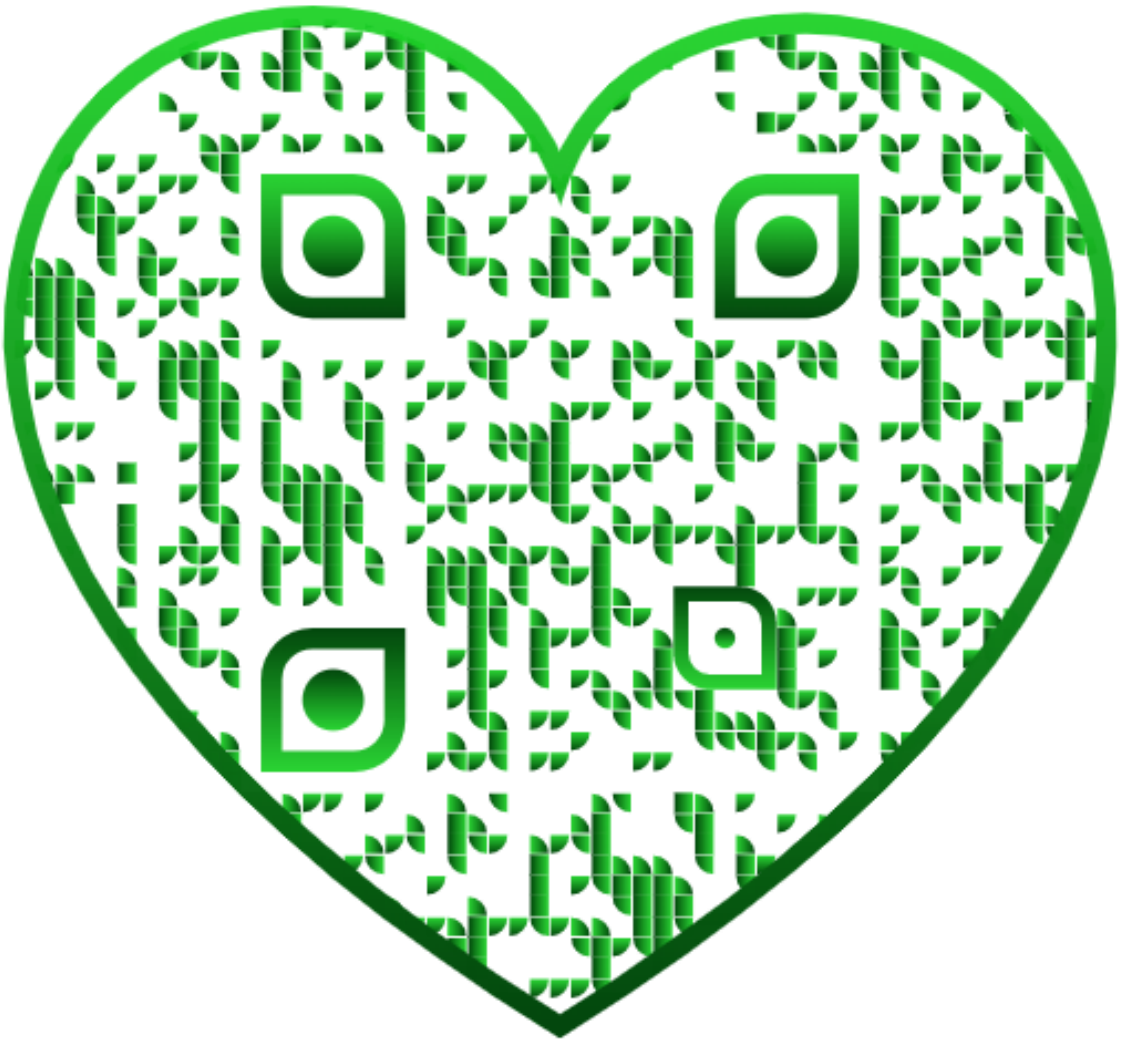
Colloids



Introduction, Colloidal Systems

- Fundamental interfacial and electrical properties of colloids and small particles, Helpful in understanding of pharmaceutical disperse systems,
- Three types of disperse systems: molecular, colloidal, and coarse dispersions,
- The only difference between these three systems is the size of the dispersed phase and not its composition,

Definitions:

- Colloidal ~ a small size that are floating in a medium,
  - Systems with particles dispersed in a medium, but are not dissolved,
  - If left undisturbed, the dispersed particles will not settle or form sediment.
- Particles that measure from 10 to 10,000 angstroms (or 1 to 1000 nm)
- Dispersed systems
  - Colloids vs Solutions
  - Colloids vs (Emulsions and Suspensions)

- Size limits are arbitrary,
- There being no distinct transition
- Mean particle diameter?

Property	Molecular Dispersions	Colloidal Dispersions	Coarse Dispersions
Particle size	< 1nm	1 – 1000nm	>1000nm
Nature	Homogeneous	Heterogeneous	Heterogeneous
Filterability	Particles diffuse rapidly through filter paper as well as parchment paper.	Pass through filter paper but not through parchment paper.	Pass through filter paper and parchment paper.
Visibility	Particles are not visible to naked eye.	Particles are not seen to naked eye but can be studied through ultra-microscope.	Particles are big enough to be seen by naked eye.
Tyndall effect	Does not show Tyndall effect.	Show Tyndall effect.	May or may not show Tyndall effect.
Appearance	Transparent	Translucent	Opaque

Types of colloidal systems

- Depending upon the state of dispersed phase and dispersion medium:
  - Foam
  - Solid foam
  - Liquid Aerosol
  - Emulsions
  - Gels
  - Solid Aerosol
  - Sol (Colloidal suspension)
  - Solid sol (Solid suspension)

Dispersion Medium	Dispersed Phase	Type of colloid	Example
Gas	Liquid	Aerosol	Fog, mist
Gas	Solid	Aerosol	Smoke
Liquid	Gas	Foam	Whipped cream
Liquid	Liquid	Emulsion	Mayonnaise, hair cream
Liquid	Solid	Sol	Paints, cell fluids
Solid	Gas	Foam	Pumice, plastic foams
Solid	Liquid	Gel	Jelly, cheese
Solid	Solid	Solid Sol	Ruby glass (glass with dispersed metal)

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- Based on the nature of interaction between dispersed phase and dispersion medium:

1) Lyophilic Colloids

- Containing colloidal particles that interact to an appreciable extent with the dispersion medium,
- The dispersed phase does not precipitate easily and the sols are quite stable,
- Example: The dissolution of acacia or gelatine in water

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2) Lyophobic Colloids

- Composed of materials that have little attraction, if any, for the dispersion medium
- Generally composed of inorganic particles dispersed in water,
- Dispersion can be achieved by the use of high intensity ultrasonic, colloidal mills, and condensation/aggregation,
- Lyophobic sols are not stable, and need stabilizing agents.
- Example: gold, silver, sulfur, arsenous sulfide, and silver iodide

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3) Association or Amphiphilic colloids

- This class of colloids is based on type of particles of the dispersed phase,
- Certain substances behave as strong electrolytes at low concentration but at higher concentrations exhibit colloidal characteristics due to the formation of aggregated particles (micelles).
- Such substances are amphiphiles (SAAs)
  - Are characterized by having two distinct regions of opposing solution affinities within the same molecule or ion,

- At low concentration: the amphiphiles exist separately,
- As the concentration is increased: aggregation occurs over a narrow concentration range,
  - The concentration of monomers at which micelles form is termed as critical micelle concentration (CMC)
  - The number of monomers that aggregate to form micelle is known as the aggregation number of the micelles

Colloidal Particle Properties

1. Optical Properties

a) The Faraday–Tyndall Effect

- When a strong beam of light is passed through a colloidal sol, a visible cone, resulting from the scattering of light by the colloidal particles, is formed.

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b) Electron Microscope

- Capable of yielding pictures of the actual particles,
- Used to observe the size, shape, and structure of colloidal particles.
  - Due to its high resolving power
  - Which is characterized by 'd' ~ the smallest distance by which two objects are separated and yet remain distinguishable.

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c) Light Scattering

- Depends on the Faraday–Tyndall effect
- Used for determining the molecular weight of colloids
- It's described in terms of **turbidity**.
  - Turbidity (τ) ~ fractional decrease in the intensity of incident light (due to scattering) when it passes through 1 cm of solution.

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- Turbidity can also be expressed by:

$$\tau = \frac{Intensity\ of\ scattered\ light\ (I_s)}{Intensity\ of\ insident\ light\ (I)}$$

- The turbidity can then be calculated from the intensity of the scattered light,

- The molecular weight of the colloid can be obtained from:

$$\frac{Hc}{\tau} = \frac{1}{M} + 2Bc$$

- c – concentration
- τ – wave length
- M – Molecular wt.
- H – constant for a given system
- B – interaction constant

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- Light scattering can also be used to determine the molecular weight of colloidal aggregates and micelles:
  - The above equation can be modified to estimate the molecular weight of micelles:

$$\frac{H(c - c_{CMC})}{(\tau - \tau_{CMC})} = \frac{1}{M} + 2B(c - c_{CMC})$$

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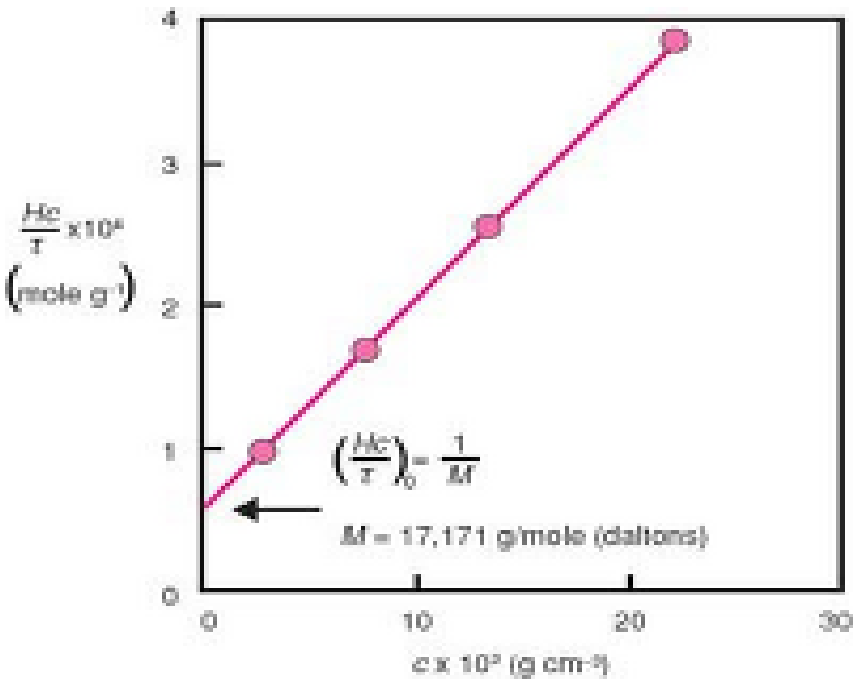
- Note:
  - A plot of ($\frac{Hc}{\tau}$ vs. c) give a straight line with slop "B" and intercept "$\frac{1}{M}$"



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2. Kinetic Properties of Colloids

- Properties related to the motion of particles with respect to the dispersion medium,
- The motions may be:
  - Thermally induced (Brownian movement, Diffusion, Osmosis),
  - Gravitationally induced (sedimentation), or applied externally (viscosity).
  - Electrically induced (described later)

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a) Brownian Motion

- Random movement of colloidal particles,
- Resulting from the bombardment of the particles by the molecules of the dispersion medium,
- The velocity is inversely related to particle size and viscosity, and directly related with temperature.

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b) Diffusion

- Definition?
- Fick's first law?

$$\frac{dQ}{dt} = -DS\frac{dC}{dx}$$

Where; D ~ diffusion coefficient, S ~ surface area, dc/dx ~ concentration gradient, dq/dt ~ amount of substance diffusing in time

- If the colloidal particles can be assumed to be approximately spherical,
  - **Sutherland-Einstein eq**. can be used to obtain the radius and molecular weight of the particle:

$$D = \frac{kT}{6\pi\eta r} \qquad \text{OR} \qquad D = \frac{RT}{6\pi\eta rN}$$

Where; k is the Boltzmann constant, R is the molar gas constant, T is the absolute temperature, η is the viscosity of the solvent, r is the radius of the spherical particle, and N is Avogadro's number.

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c) Osmotic Pressure

- van't Hoff equation:

$$\pi = cRT$$

- Where; where c is molar concentration of solute,

- Can be used to calculate the molecular weight of a colloid in a dilute solution:

$$\pi = \frac{c_g}{M} RT \text{ , where } c = \frac{c_g}{M}$$

- c_g ~ grams of solute per litter of solution and
- M ~ molecular weight

- The equation, $\pi = \frac{c_g}{M} RT$, can be re-written as:

$$\frac{\pi}{c_g} = \frac{RT}{M}$$

holds only for ideal solutions (low conc. of spherocolloids)

- $\frac{\pi}{c_g}$ is often a linear function of c_g

- Accordingly, the above equation can be modified:

$$\frac{\pi}{c_g} = RT\left(\frac{1}{M} + Bc_g\right)$$

  - Where; where B is a constant for any particular solvent/solute system

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d) Sedimentation

- Stokes's law (for sedimentation of spherical particles of about 0.5 μm):

$$v = \frac{2r^2(\rho - \rho_0)g}{9\eta_0}$$

  - v ~ velocity
  - r ~ particle radius
  - ρ & ρ_0 ~ densities
  - η ~ medium viscosity
  - g ~ gravitational force

- Particles showing Brownian movement, sedimentation aided by ultracentrifuge:

$$v = \frac{dx}{dt} = \frac{2r^2(\rho - \rho_0)\omega^2 x}{9\eta_0}$$

  - ω ~ angular velocity
  - x ~ distance particle move from center

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e) Viscosity

- Used to express the resistance to flow of a colloidal system under an applied stress.
- Can be used to obtain the molecular weight and to provide information regarding the shape of the particles.
- Einstein equation (for dilute colloidal dispersions of spherical particles):

$$\eta = \eta_0(1 + 2.5\phi)$$

- η_0 ~ viscosity of Disp. Medium
- η ~ viscosity in the presence of colloidal particles

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3. Electrical Properties of Colloids

- Particle surface charges affect colloidal properties.
- Interfacial Phenomena (?)
- 'Zeta' (electrokinetic) potential (?)
- 'Nernst' (electrothermodynamic) potential (?)

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a) Electrokinetic Phenomena

- **Electrophoresis:** movement of a charged particle through a liquid under the influence of an applied potential difference,
- **Electroosmosis:** liquid moves relative to the charged surface,
- **Sedimentation potential:** the reverse of electrophoresis, is the creation of a potential when particles undergo sedimentation,
- **Streaming potential:** forcing a liquid to flow through a plug or bed of particles creates the potential.

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b) Stability of Colloid Systems

- The presence or absence of a charge on a colloidal particle is an important factor in the stability of colloidal systems,
- Stabilization may be achieved by:
  - Providing the dispersed particles with an electric charge (stabilization by electrostatic repulsion),
  - Stabilization of a lyophobic sol by steric hindrance,
  - Surrounding each particle with a protective solvent sheath (for lyophilic sols)

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- **Stabilization by electrostatic repulsion:**
  - When two uncharged hydrophobic particles are in close proximity, they attract each other by Vander Waals forces.
  - These forces decrease with increasing distance between particles.
  - Coagulation occurs as the primary particles aggregate into increasingly large secondary particles or flocks.
  - If the dispersion consists of two kinds of particles with positive and negative charges, the electrostatic attraction between oppositely charged particles is superimposed on the attraction by van der waals forces, and coagulation is accelerated

- Schulze–Hardy rule
  - The valence of ions having a charge opposite to that of the particles appears to determine the effectiveness of the electrolyte in coagulating the colloid.
  - The precipitating power increases rapidly with the valence or charge of the ions
- DLVO theory
  - The forces on colloidal particles in a dispersion are due to electrostatic repulsion and London-type van der Waals attraction

- Coacervation

  - When negatively and positively charged hydrophilic colloids are mixed, the particles may separate from the dispersion to form a layer rich in the colloidal aggregates (coacervates),

  - The phenomenon may result in physical incompatibility

  - E.g. Mixing of gelatine and acacia at a pH below 4.7

- Stabilization of lyophobic vs lyophilic colloids:
  - A lyophobic solution is thermodynamically unstable,
    - Particles are stabilized only by the presence of electrical charges on their surfaces,
    - Addition of a small amount of electrolyte tends to stabilize the system,
    - The like charges produce a repulsion that prevents coagulation of the particles
    - But, addition of larger amount sometimes results in the accumulation of opposite ions and reduces the zeta potential below its critical value and coagulation will occur.

- Lyophilic and association colloids are thermodynamically stable,
  - Exist in true solutions so that the system constitutes a single phase.
  - When negatively and positively charged hydrophilic colloids are mixed, the particles may separate from the dispersion to form a layer rich in the colloidal aggregates (coacervation).

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- **Stabilization by steric hindrance:**
  - Non-ionic polymeric and surface active materials adsorbed at the particle surface can stabilize a lyophobic sol,
  - Resulting in a steric interaction when the layers over lap leading to repulsion,
  - The particles do not approach each other closer than about twice the thickness of the adsorbed layer.

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c) Sensitization and Protection

- **Sensitization**
  - The addition of small amount of hydrophilic or hydrophobic colloid to a hydrophobic colloid of opposite charge tends to sensitize or even coagulate the particles
  - This is due to reduction of zeta potential below the critical value,
  - Stability is ineffective because of low surface coverage with adsorbed polymers.

- By Bridging:
  - In case of non-ionic or poly electrolytes with charges of the same sign as the sol,
  - At low polymer concentration there are no enough polymers present to cover each sol particle completely,
  - A single macromolecule may be adsorbed on two particles, bridging the gap between them and pulling them close together,
  - Flocks of several particles may be formed with bridging of several particles.

- By neutralization of the charge:
  - If the polymer has ionic groups of charge opposite to the charge of sol particle,
  - Limited adsorption neutralizes the charge of the particles, reducing the zeta potential to near zero,
  - Because of low surface coverage stabilization is not effected by protective effect.

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- Protection
  - Stabilizing a hydrophobic colloid by addition of large amounts of hydrophile.
  - The added hydrophilic sol is known as a protective colloid.
  - The protective property is expressed most frequently in terms of the 'gold number'

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4. Solubilization

- A property of association colloids (Micelles) to increase the solubility of materials/drugs that are normally insoluble, or only slightly soluble,

- The location, distribution, and orientation of solubilized drugs in the micelle is important:

  - Determine the kinetic aspect of the solubilization process and the interaction of drugs is important,

  - May also affect the stability and bioavailability of the drug

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- For successful formulation of solubilized systems, the following factors to be considered:
  - Concentration (of the SAA)
    - Toxicity ~ If to be taken internally
    - Efficiency ~ if excess is used, reduced absorption and activity; an insufficient amount can lead to precipitation of the solubilized material
  - Miscibility with the solvent (usually water)
  - Compatible, and odour and taste